Kidney Disease in Your Patients with Diabetes: An Opportunity for Prevention

DOH Diabetes Kidney Screening and Treatment Task Force (authors/affiliations listed at end of article)

Diabetes affects approximately 16 million people in the United States but only 10 million are aware that they have the disease.[1,2] Kidney disease affects 20-40% of persons with diabetes and diabetic nephropathy is now the leading cause of end-stage renal disease, or dialysis dependence, in the US. Interventional studies suggest that early treatment of hyperglycemia,[3-6] hypertension[7-9] and microalbuminuria[7,10-14] slows the progression of diabetic nephropathy. Treatment may also delay the need for dialysis and perhaps even prevent diabetic nephropathy occurrence in both Type 1 and Type 2 diabetes. Multiple studies in both Type 1 and Type 2 diabetic patients have shown that the use of angiotensin converting enzyme inhibitors (ACE-Inhibitors)[3,14] and angiotensin receptor blockers (ARBs)[15-16] decreases progression of overt diabetic nephropathy and improves outcomes.

- Primary care providers, including family physicians, have the most frequent contact with diabetic patients and therefore the greatest potential to impact their health.
- Over 200,000 people in Washington have diabetes.
- Approximately 20-45% of people with diabetes will develop diabetic nephropathy, which is dependent upon the type and duration of diabetes.
- Each day in Washington, one person with diabetes begins dialysis.
- In a given year, fewer than 40% of people with diabetes in Washington receive screening for kidney function (Department of Health Audit, 1999)

Due to the complex nature of diabetes, the preventable nature of most complications and the magnitude of associated health care costs, the Washington State Department of Health developed a program of statewide public health surveillance and control activities for patients with diabetes. This collaborative evaluation of private and public health care systems found that evaluation of kidney function (testing of any kind) was being done in less than 40% of individuals with diabetes in the state, regardless of insurance type. In response to this audit, the Department of Health's Diabetes Control Program undertook a number of quality improvement projects, one of which included the formation of the Kidney Screening and Treatment Task Force. The Task Force, which included representatives from the medical and scientific laboratory communities in Washington, evaluated preexisting protocols for the screening and treatment of diabetic nephropathy from the American Diabetes Association and National Kidney Foundation. These protocols were expanded to include more preventive measures which were based upon current evidence from the literature. Two algorithms, which summarize these recommendations (flow sheet and table formats), are included here and are available in color format along with more detailed explanations and a clinical bibliography at the website of the Washington State Diabetes

Collaborative: www.doh.wa.gov/cfh/wsdc.

A Closer Look at the Algorithms:

Urinalysis for protein:

A routine urinalysis should be performed in all Type 2 diabetic patients at the time of diagnosis and in Type 1 patients with a diagnosis of diabetes for 5 years or more. The urine dipstick detects a variety of proteins, although it is most sensitive to albumin. A patient with a negative dipstick (less than 1+ protein or ~30 mg/dL) should be monitored annually with a more specific test for microalbuminuria. A patient with proteinuria (dipstick showing 1+ or greater than ~30 mg/dl protein) should be monitored with a 24-hour urine collection for total protein.

- Is the dipstick less than 1+ for protein? If this patient is already on an ACE-Inhibitor or an ARB, potassium and creatinine should be measured; if either is abnormal, the primary physician should consider consulting with a nephrologist. If both tests are normal the patient should be continued on an ACE-Inhibitor or ARB, and have annual creatinine and potassium levels in addition to an annual urinalysis or microalbuminuria test to measure the progression of proteinuria. Furthermore, recent studies suggest that dual blockade of the renin-angiotensin system with an ACE-inhibitor and ARB is more effective in reducing blood pressure and albuminuria compared to either agent alone.[17] However, care should be exercised in patients with renal insufficiency. In addition to the above recommendations, Protective Recommendations for blood pressure control, glycemic control, lipid evaluation and lipid treatment should be considered. Patients not on ACE-inhibitors or ARBs should be retested for **micro**albuminuria annually. Patients on these agents can be tested annually to insure microalbuminuria has not progressed, although annual testing in this group remains controversial.
- Is the dipstick 1+ or greater for protein? This patient has "macroalbuminuria" and should be assessed with a measurement of total urine protein to quantitate the level of all the urine proteins present, which includes albumin. If the level of total protein is greater than 1 gm/24 hr, referral to a nephrologist is recommended.

Testing for albuminuria:

There are several options for microalbuminuria testing, some of which include a random (spot) urine albumin (or protein) to creatinine ratio (reported as mg albumin/mg creatinine or without units), a 24-hour urine collection that measures total mg of albumin in 24-hours (g/24hours) and a timed urine collection (reported as mg albumin/min). Although the

American Diabetes Association Protective Guidelines:

- **Strict blood pressure control of less than or equal to 130/80 mm/hg.**
- **Strict glucose control measured by an HbA1C less than or equal to 7.0% (using an NGSP-certified method).**
- **Lipid monitoring and control with a goal of total cholesterol less than 200 mg/dL, HDL greater than 45 mg/dL, LDL less than 100 mg/dL and triglycerides less than 150 mg/dL.[19]**

gold standard for screening has historically been the 24-hour collection, spot urine collections for albumin and creatinine can provide accurate information, and are often the easiest test to accomplish in the outpatient setting. First void or morning collections are preferred because of diurnal variation in albumin excretion. If the first voided specimen cannot be obtained, then urine should be collected at approximately the same time of day for repeated collections in the same individual.

- Because of the marked day-to-day variability in albumin excretion, and the potential for transient elevations in urine albumin excretion, it is recommended that two of three collections within a 3-month period show microalbuminuria. Confounding factors associated with an increase in microalbuminuria include poorly controlled diabetes, morbid obesity, acute illness with fever, pregnancy, high protein diet, urinary tract infection, congestive heart failure, acute water consumption (more than one liter), hematuria, menstruation, certain medications (non-steroidal anti-inflammatory drugs, calcium channel blockers) or major stress such as surgery or anesthesia.[18] Semiquantitative assays for albumin are available as test strips. These assays measure albumin concentration, so dilute urines or intra-individual variances in albumin excretion may yield a false-negative result. Semiquantitative assays are convenient and may be suitable for screening with the above caveats noted. These assays however, are not sufficiently accurate for regular monitoring of patients.

- Laboratory results can be presented in a variety of ways, which may depend upon the collection sample used. Some laboratories may still report normals or a reference range for microalbuminuria that was based on an assessment of a "normal" population.

Turn to the center of this issue for a full color chart and diagram summarizing screening and treatment of diabetic nephropathy.

When to consider consultation or referral:

An important part of the screening and treatment algorithms is the recommendation for consulting or referring to a nephrologist. A patient whose quantitative urine protein test shows greater than one gram a day of protein or greater than one gram of protein per gram of creatinine requires referral to a specialist to determine the cause of the kidney disease, as there may be causes other than diabetes. The nephrologist can discuss treatment options and educate the patient regarding the potential for dialysis. If the total protein does not exceed the above threshold, but the potassium and/or creatinine are abnormal, consultation with a nephrologist is recommended.

What you as a family practitioner can do to protect the kidney function of your patients with diabetes:

- Strive for the American Diabetes Association Protective Guidelines goals for your patients.

- Strict blood pressure control of less than or equal to 130/80 mm/hg.

- Strict glucose control measured by an HbA1C less than or equal to 7.0% (using an NGSP-certified method).

- Lipid monitoring and control with a goal of total cholesterol less than 200 mg/dL, HDL greater than 45 mg/dL, LDL less than 100 mg/dL and triglycerides less than 150 mg/dL.[19]
- Screen your patients for kidney disease.
- Determine your true rate of kidney screening by a brief chart review of the last five diabetic patients you have seen. If your patients have not been screened for kidney disease, consider what might be contributing to less than optimum testing. If you find you are testing and treating appropriately, how have you accomplished it? Share your method with others.
- Build on what you are already doing to help your patients manage their disease. If they are checking and recording their blood glucose and checking their feet, teach them to track their kidney function tests as well. Consider the use of over-the-counter home microalbuminuria tests.
- Ask your laboratory colleagues to develop consistency in reports and to help you understand the results they are reporting to you. Labs may report results in a variety of ways, e.g., "normal" or "clinical albuminuria." Labs may have the capacity to incorporate messages with the results, e.g. "UA positive for protein; recommend quantitate total protein with 24 hour test or spot a.m. urine." If microalbuminuria does not appear as a test on the lab slips you use, your lab may be able to help you to change the ordering form to make the process easier.
- Develop consulting relationships with colleagues.
- As noted above, your colleagues in the lab can provide valuable information in many aspects of care, beyond the reporting of results. Call upon them to work with you and your patients to improve care and outcomes.
- An important component is consultation with and referral to specialists in diabetic care such as diabetologists and nephrologists. The evidence-based screening and treatment algorithm was developed with the input of primary care physicians, diabetologists and nephrologists, and reflects their collective recommendations for both consultation and referral.

For more information, visit the Washington State Diabetes Collaborative website at www.doh.wa.gov/cfh/wsdc.

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